

## Therapeutic Class Overview

### Ophthalmic Corticosteroids

#### INTRODUCTION

- Most ophthalmic corticosteroids are indicated to treat various steroid-responsive inflammatory ocular conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe such as allergic conjunctivitis, acne rosacea, superficial punctate keratitis, herpes zoster keratitis, iritis, and cyclitis. Other indications include postoperative inflammation following various ocular surgeries; anterior uveitis; ocular allergies; corneal injury from chemical, radiation or thermal burns; and penetration of foreign bodies.
  - Dexamethasone sodium phosphate solution is also approved for otic use; however, this review will only cover ophthalmic indications.
- Ocular corticosteroids are thought to act by the induction of phospholipase A<sub>2</sub> inhibitory proteins; these proteins control the biosynthesis of inflammatory mediators (eg, prostaglandins and leukotrienes) by inhibiting the release of the common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A<sub>2</sub> (*Facts & Comparisons 2018*).
  - Steroids inhibit edema, cellular infiltration, fibrin deposition, capillary dilation, leukocyte migration, capillary and fibroblast proliferation, collagen deposition, and scar formation associated with inflammation.
- So-called “soft” ophthalmic corticosteroids (eg, loteprednol etabonate, fluorometholone, rimexolone [discontinued in the US]) have been designed with certain structural modifications in an effort to retain anti-inflammatory efficacy, while reducing the risk of typical corticosteroid adverse effects (AEs). Soft corticosteroids are metabolized at the target site or near the application site and are claimed to produce a low rate of AEs in relation to their anti-inflammatory potency (*Bielory et al 2010, Hamrah et al 2018, Pleyer et al 2002*).
- Ophthalmic steroids are available in various formulations including emulsions, ointments, solutions, and suspensions. Dexamethasone, fluorometholone, prednisolone acetate, and prednisolone sodium phosphate are currently available generically.
  - Prednisolone acetate 1% is available as 2 different branded products, Pred Forte, which contains both benzalkonium chloride (BAK) preservative and the inactive ingredient, sodium bisulfite, and Omnipred, which contains BAK preservative, but is free of sulfites (*Prescribing information: Omnipred 2007, Pred Forte 2017*).
  - Unlike all of the other commercially available corticosteroid ophthalmic drops, difluprednate does not contain BAK preservative (*Foster et al 2010*).
  - Fluorometholone differs structurally from other traditional corticosteroids in that it lacks a hydroxyl group in the 21st position; it undergoes local ocular metabolism in the cornea (*McGhee et al 2002*).
  - Loteprednol etabonate is a unique corticosteroid molecule that is structurally similar to other corticosteroids (eg, prednisolone), but has an ester group substituted for a ketone at the C-20 position, which results in a predictable transformation to an inactive metabolite (*Bielory et al 2010*).
  - Ointments are particularly useful for overnight treatment as an adjunct to daytime drops in certain inflammatory conditions (*McGhee et al 2002*). Disadvantages of ointments include transient blurred vision and more difficult administration (*Comstock et al 2011*).
- Medispan class: Ophthalmic steroids

**Table 1. Medications Included Within Class Review**

Drug	Generic Availability
Maxidex (dexamethasone ophthalmic suspension, 0.1%)	-
dexamethasone sodium phosphate ophthalmic solution, 0.1%	✓
Durezol (difluprednate ophthalmic emulsion, 0.05%)	-
FML (fluorometholone ophthalmic suspension, 0.1%)	✓
FML (fluorometholone ophthalmic ointment, 0.1%)	-
FML Forte (fluorometholone ophthalmic suspension, 0.25%)	-

Data as of April 9, 2018 AVD/AS

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Drug	Generic Availability
Flarex (fluoromethalone acetate ophthalmic suspension, 0.1%)	-
Alrex (loteprednol etabonate ophthalmic suspension, 0.2%)	-
Lotemax (loteprednol etabonate ophthalmic suspension, 0.5%)	-
Lotemax (loteprednol etabonate ophthalmic gel, 0.5%)	-
Lotemax (loteprednol etabonate ophthalmic ointment, 0.5%)	-
Pred Mild (prednisolone acetate ophthalmic suspension, 0.12%)	-
Omnipred, Pred Forte (prednisolone acetate ophthalmic suspension, 1%)	✓
prednisolone sodium phosphate ophthalmic solution, 1%	✓

(Drugs @FDA 2018, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations 2018)

## INDICATIONS

**Table 2. Food and Drug Administration Approved Indications**

Indication	Maxidex (dexamethasone suspension); dexamethasone solution	Durezol (difluprednate)	FML, FML Forte (fluorometholone); Flarex (fluoromethalone acetate)	Alrex, Lotemax (loteprednol etabonate)	Pred Mild, Pred Forte, Omnipred (prednisolone acetate)	prednisolone sodium phosphate
Anterior uveitis, endogenous		✓				
Corneal injury from chemical, radiation or thermal burns	✓				✓ (Omnipred)	✓
Mild to moderate noninfectious allergic and inflammatory disorders of the lid, conjunctiva, cornea, and sclera (including chemical and thermal burns)					✓ (Pred Mild)	
Penetration of foreign bodies	✓				✓ (Omnipred)	✓
Postoperative inflammation and pain following ocular surgery		✓		✓ (Lotemax gel, ointment)		
Postoperative inflammation following ocular surgery				✓ (Lotemax suspension)		
Temporary relief of the signs and				✓ (Alrex)		

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Indication	Maxidex (dexamethasone suspension); dexamethasone solution	Durezol (difluprednate)	FML, FML Forte (fluorometholone); Flarex (fluoromethalone acetate)	Alrex, Lotemax (loteprednol etabonate)	Pred Mild, Pred Forte, Omnipred (prednisolone acetate)	prednisolone sodium phosphate
symptoms of seasonal allergic conjunctivitis						
Steroid-responsive inflammatory ocular conditions	✓ *		✓ *	✓ * (Lotemax suspension)	✓ * (Pred Forte, Omnipred)	✓ *

\*Indicated for the treatment of steroid-responsive inflammatory ocular conditions of the palpebral and bulbar conjunctiva, cornea and anterior segment of the globe, such as allergic conjunctivitis, acne rosacea, superficial punctate keratitis, herpes zoster keratitis, iritis, cyclitis and selected infective conjunctivides when the inherent risk of steroid use is accepted to obtain a diminution in edema and inflammation.

(Prescribing information: Alrex 2016, dexamethasone sodium phosphate 2016, Durezol 2017, Flarex 2017, FML ointment 2013, FML suspension 2013, FML Forte 2013, Lotemax gel 2016, Lotemax ointment 2011, Lotemax suspension 2016, Maxidex 2017, Omnipred 2007, Pred Forte 2017, Pred Mild 2017, prednisolone sodium phosphate 2013)

- Information on indications, mechanism of action, pharmacokinetics, dosing, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

#### CLINICAL EFFICACY SUMMARY

- Two double-blind (DB), multi-center (MC), randomized, active-controlled (AC) trials (*Loteprednol etabonate US Uveitis Study Group 1999*) compared the safety and efficacy of loteprednol etabonate 0.5% suspension with that of prednisolone acetate 1% suspension in reducing the ocular signs and symptoms associated with acute anterior uveitis. The first study involved up to 42 days of treatment, starting with a dose of 8 times per day. The second study involved up to 28 days of treatment, starting with a dose of 16 times per day. Efficacy was evaluated by the proportion of patients with anterior chamber cell score of 0 for key signs and symptoms of uveitis.
  - In Study 1 (N = 70), the proportion of patients achieving resolution of anterior chamber cell by the final visit was 74% for loteprednol etabonate vs 88% for prednisolone acetate (p = 0.194). In Study 2 (N = 175), the proportion of patients achieving resolution of anterior chamber cell by the final visit was 72% for loteprednol etabonate vs 87% for prednisolone acetate (p = 0.015).
  - In both studies, an intraocular pressure (IOP) increase > 10 mm Hg was observed in 7 patients receiving prednisolone acetate and 1 patient receiving loteprednol etabonate.
- A DB, MC, randomized, non-inferiority trial (N = 90) (*Foster et al 2010*) compared the safety and efficacy of difluprednate 0.05% emulsion dosed 4 times daily with prednisolone acetate 1% suspension dosed 8 times a day for the treatment of endogenous anterior uveitis. At day 14, mean anterior chamber cell grade improvement for difluprednate-treated patients was similar to that observed with prednisolone-treated patients (2.1 vs 1.9, respectively), demonstrating non-inferiority. Clinically significant IOP elevation occurred in 3 difluprednate-treated patients (6.0%) and 2 prednisolone-treated patients (5.0%).
- A DB, MC, AC, randomized, non-inferiority trial (N = 110) (*Sheppard et al 2014*) compared the efficacy of difluprednate 0.05% emulsion dosed 4 times daily with prednisolone acetate 1% suspension dosed 8 times a day or the treatment of endogenous anterior uveitis. At day 14, the mean change in anterior chamber cell grade with difluprednate was noninferior to that of prednisolone acetate (-2.2 vs -2.0, respectively; p = 0.16). There was a statistically significant difference in mean IOP increase at day 3 (2.5 mm Hg for difluprednate-treated patients vs 0.1 mm Hg for prednisolone acetate-treated patients, p = 0.0013), but not at other time points during the study.

- A DB, randomized controlled trial (RCT) (*Stewart 2004 [abstract]*) compared fluorometholone acetate 0.1% (Flarex) suspension with loteprednol etabonate 0.5% suspension in 30 patients undergoing cataract extraction. The treatment regimen for both groups included instillation of 1 drop 4 times daily for 14 days. Flare scores gradually decreased during the course of the study. On day 21, no flare was observed in any of fluorometholone patients while 3 loteprednol patients still showed signs of flare. However, no statistically significant differences in flare, anterior segment cell, or conjunctival hyperemia scores were observed between the 2 groups.
- An investigator-masked, MC, RCT (N = 88) (*Lane et al 2013*) evaluated the efficacy of loteprednol etabonate 0.5% 4 times daily vs prednisolone acetate 1% 4 times daily for the control of postoperative inflammation after cataract surgery. Throughout the 3-week follow-up, control of inflammation was equivalent between the treatment groups. Mean IOP was numerically higher in patients treated with prednisolone acetate vs loteprednol etabonate at each assessment; however, there were no statistically significant differences between the 2 groups.
- A DB, MC, randomized, contralateral-eye trial (N = 52) (*Donnenfeld et al 2011*) compared the effects of difluprednate 0.05% vs prednisolone acetate 1% suspension on corneal thickness and visual acuity after cataract surgery. The first eye randomly received 1 of the treatment drugs; the fellow eye received the alternative. At day 1, corneal thickness was 33  $\mu\text{m}$  less in the difluprednate-treated eyes ( $p = 0.026$ ). The mean IOP remained within the normal range for both groups at all study visits.
- A DB, MC, RCT (N = 73) (*Raizman et al 2007*) comparing 2 ophthalmic prednisolone acetate 1% formulations (Omnipred and Pred Forte) in adult patients who underwent cataract surgery found that there were no statistically significant differences in clinical efficacy between the treatment groups in terms of postoperative ocular pain, keratitis, aqueous cell counts, or aqueous flare on post-op days 1, 12, and 28.
- An investigator-masked, randomized study (N = 60) (*Oner et al 2012*) evaluating the safety and efficacy of loteprednol etabonate 0.5%, prednisolone acetate 1%, and fluorometholone acetate 0.1% for the treatment of vernal keratoconjunctivitis found that the baseline mean scores of signs and symptoms gradually improved for all groups except for pannus formation in the fluorometholone group; however, all signs and symptoms (with the exception of chemosis) were significantly less improved in the fluorometholone group compared to the other treatments. There was significant IOP elevation in the prednisolone group after the day 3 visit.

## CLINICAL GUIDELINES

- **American Academy of Ophthalmology: Cataract in the Adult Eye Preferred Practice Pattern** (*Olson et al 2017*)
  - Postoperative follow-up
    - Postoperative regimens of topically applied antibiotics, corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), and oral analgesics vary among practitioners. Optimal regimens for the use of these agents have not been established; thus, the operating surgeon is responsible for making the decision whether to use any or all of the topical products alone or in combination.
    - Elevated IOP is a postoperative complication with corticosteroids.
  - Cystoid macular edema
    - Topical anti-inflammatory agents are used to prevent as well as to treat cystoid macular edema.
    - There is evidence that NSAIDs, alone or in combination with topical corticosteroids, decreases the risk of postoperative cystoid macular edema.
- **American Optometric Association: Care of the Adult Patient with Cataract** (*Murrill et al 2004*)
  - A combination of topical and oral anti-glaucoma, antibiotic, and anti-inflammatory medications may be administered to the patient before, during, and after an operation.
  - Topical corticosteroids may be used to suppress inflammation associated with cataract surgery.
  - To control inflammation associated with anterior uveitis, topical corticosteroids such as prednisolone acetate 1% may be used every 2 to 4 hours depending on the degree of inflammation.
  - When there is anterior chamber inflammation associated with cystoid macular edema, topical steroidal and nonsteroidal anti-inflammatory agents should be applied to the eye for up to a month.
- **American Academy of Ophthalmology: Refractive Errors & Refractive Surgery Preferred Practice Pattern** (*Chuck et al 2018*)
  - Surface ablation techniques
    - Postoperative regimens of topically applied antibiotics, corticosteroids, and oral analgesics vary among practitioners. It is the decision of the surgeon to use any or all of these products alone or in combination.
    - Topical corticosteroids are generally started immediately after surgery and tapered over a period of days to weeks, and sometimes months.

- Periodic examinations are necessary to monitor ocular status and to check for corticosteroid-related side effects such as elevated IOP.
- Laser in situ keratomileusis
  - Corticosteroids are generally used for a short time postoperatively.
  - Treatment of diffuse lamellar keratitis is commonly guided by the severity of the inflammation. Increasing the frequency of topical corticosteroid administration with a closer follow-up is practiced by most surgeons.
- **American Optometric Association: Care of the Patient with Anterior Uveitis** (*Alexander et al 2004*)
  - Available treatment options for the treatment of anterior uveitis include: topical ophthalmic corticosteroids, cycloplegics and mydriatics, oral steroids and NSAIDs, and other therapies such as immunosuppressants.
    - Steroids should be continued until the cellular reaction is minimal or absent, and then they should be tapered. The more potent and frequent the use of a topical steroid, the longer the tapering period required.
- **American Academy of Ophthalmology: Conjunctivitis Preferred Practice Pattern** (AAO 2013a)
  - Seasonal allergic conjunctivitis
    - Mild allergic conjunctivitis can be treated with an over-the-counter (OTC) antihistamine/vasoconstrictor or second-generation topical histamine H<sub>1</sub>-receptor antagonist. If the condition is persistent, mast-cell stabilizers may be used.
    - A brief course (1 to 2 weeks) of a low-potency topical corticosteroid may be added if the symptoms are not adequately controlled. The lowest potency and frequency of corticosteroid administration that relieves the patient's symptoms should be used. If corticosteroids are used in chronic or recurrent conjunctivitis, periodic exams should be performed to monitor for cataract and glaucoma.
    - Ketorolac, an NSAID, is also approved for the treatment of allergic conjunctivitis. Additional measures include allergen avoidance and using cool compresses, oral antihistamines, and artificial tears.
  - Vernal/atopic conjunctivitis
    - General treatment measures include modifying the environment to minimize exposure to allergens or irritants and using cool compresses and ocular lubricants. Topical and oral antihistamines and topical mast-cell stabilizers may also be beneficial.
    - For acute exacerbations, topical corticosteroids are usually necessary to control severe symptoms. The minimal amount of corticosteroid should be used based on patient response and tolerance. Topical cyclosporine is effective as adjunctive therapy to reduce the amount of topical corticosteroid used to treat severe atopic keratoconjunctivitis.
    - If corticosteroids are prescribed, baseline and periodic measurement of IOP and papillary dilation should be performed to evaluate for glaucoma and cataract.
- **American Optometric Association: Care of the Patient with Conjunctivitis** (*Quinn et al 2007*)
  - The following agents are useful in treating allergic conjunctivitis (includes atopic keratoconjunctivitis, simple allergic conjunctivitis, seasonal or perennial conjunctivitis, vernal conjunctivitis, and giant papillary conjunctivitis): topical corticosteroids, topical vasoconstrictors/antihistamines, topical antihistamines, topical NSAIDs, topical mast cell stabilizers, topical antihistamines/mast cell stabilizers, immunosuppressants, and systemic antihistamines.
    - The use of topical corticosteroids should be limited to the acute suppression of symptoms because of the potential for AEs with prolonged use (eg, cataract formation and elevated IOP).
- **American Academy of Ophthalmology: Bacterial Keratitis Preferred Practice Pattern** (AAO 2013b)
  - Ophthalmic corticosteroid therapy may have a beneficial role in treating some cases of infectious keratitis due to the probable suppression of inflammation, which may reduce subsequent corneal scarring and associated visual loss.
  - Potential disadvantages of ophthalmic corticosteroid use include infection reoccurrence, local immunosuppression, inhibition of collagen synthesis predisposing to corneal melting, and increased IOP.
  - There is no conclusive evidence that ophthalmic corticosteroids alter clinical outcome.
  - Despite the risks, it is believed that the judicious use of ophthalmic corticosteroids can reduce morbidity. The minimum amount of ophthalmic corticosteroid required should be used to achieve control of inflammation.
  - Ophthalmic corticosteroids should not be used for presumed bacterial ulcers until the organism has been determined by cultures. Outcomes of corticosteroid therapy are likely to be poor for ulcers associated with *Acanthamoeba*, *Nocardia*, fungus, or herpes simplex virus.
  - IOP must be monitored frequently, and the patient should be examined within 1 to 2 days after initiation of ophthalmic corticosteroid therapy.
- **American Academy of Ophthalmology: Blepharitis Preferred Practice Pattern** (AAO 2013c)
  - Blepharitis is typically a chronic condition that cannot be cured. Optimal treatment regimens often require a trial and error approach.

- Treatments options, which are often used in combination, include the following:
  - Warm compresses
  - Eyelid hygiene
  - Antibiotics (topical and/or systemic)
  - Ophthalmic anti-inflammatory agents (eg, corticosteroids, cyclosporine)
- Ophthalmic corticosteroid eye drops or ointments are typically applied several times daily to the eyelids or ocular surface. Once the inflammation is controlled, the corticosteroid can be tapered and discontinued and then used intermittently to maintain patient comfort. The minimal effective dose should be used, and long-term therapy should be avoided if possible.
- Potential AEs of ophthalmic corticosteroid use, including the risk for developing increased IOP and cataracts may be minimized by using a site-specific ophthalmic corticosteroid such as loteprednol etabonate and ophthalmic corticosteroids with limited ocular penetration, such as fluorometholone.
- **American Academy of Ophthalmology: Dry Eye Syndrome Preferred Practice Pattern (AAO 2013d)**
  - Treatment options for patients with mild dry eye syndrome include: education and environmental modifications; discontinuation of any offending medications; aqueous enhancement using artificial tear substitutes, gels or ointments; eyelid therapy (warm compresses and eyelid hygiene); treatment of contributing ocular factors such as blepharitis or meibomianitis; and correction of eyelid abnormalities.
  - Treatments for moderate dry eye syndrome include (in addition to treatments for mild dry eye syndrome): anti-inflammatory agents (eg, topical corticosteroids and cyclosporine), systemic omega-3 fatty acid supplements, punctal plugs, and spectacle side shields and moisture chambers.
    - Low dose topical corticosteroids can be used at infrequent intervals for short-term (ie, several weeks) suppression of inflammation.
  - Treatments for severe dry eye syndrome include (in addition to treatments for mild and moderate dry eye syndrome): systemic anti-inflammatory agents, systemic cholinergic agonists, mucolytic agents, autologous serum tears, contact lenses, permanent punctal occlusion, and tarsorrhaphy.

#### SAFETY SUMMARY

- Contraindications for ophthalmic corticosteroids include hypersensitivity to any component of the formulation; most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella; mycobacterial infections of the eye; and fungal diseases of ocular structures.
  - Flarex (fluoromethalone acetate 1%), Pred Forte (prednisolone acetate 1%), and Pred Mild (prednisolone acetate 0.12%) are also contraindicated with acute purulent untreated infections.
  - Prednisolone sodium phosphate 1% solution is contraindicated after uncomplicated removal of a superficial corneal foreign body.
- Warnings and precautions for ophthalmic corticosteroids include glaucoma, cataract formation, delayed healing after cataract surgery, risk of fungal infections and secondary bacterial infections, masking or enhancement of existing bacterial infections, exacerbation of viral infections, and contact lens wear.
  - Lotemax (loteprednol etabonate 0.5%) should not be used in children following ocular surgery, as it may hinder the child's ability to see out of the operated eye.
  - Some products contain sodium bisulfite, which may cause allergic-type reactions in susceptible patients.
- AEs associated with ophthalmic steroids include glaucoma with optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, delayed wound healing, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera.

#### DOSING AND ADMINISTRATION

**Table 3. Dosing and Administration**

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Maxidex (dexamethasone, 0.1%)	Suspension	Topical ophthalmic	<u>Mild disease:</u> Up to 4 to 6 times daily  <u>Severe disease:</u> May be used hourly and tapered to	

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
			discontinuation as inflammation subsides	
dexamethasone sodium phosphate, 0.1%	Solution	Topical ophthalmic	Every hour during the day and every 2 hours during the night as initial therapy; reduce to every 4 hours when a favorable response is observed; later, further reduction to 3 to 4 times daily may suffice to control symptoms	The duration of treatment will vary with the type of lesion and may extend from a few days to several weeks.
Durezol (difluprednate, 0.05%)	Emulsion	Topical ophthalmic	<u>Anterior uveitis, endogenous</u> 4 times daily for 14 days, followed by tapering as clinically indicated  <u>Postoperative inflammation following ocular surgery</u> 4 times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the post-operative period, followed by 2 times daily for 1 week, and then a taper based on response	
FML (fluoromethalone, 0.1%)	Suspension	Topical ophthalmic	2 to 4 times daily; during the initial 24 to 48 hours, the frequency may be increased to every 4 hours	Care should be taken not to discontinue therapy prematurely.  If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.
FML (fluoromethalone, 0.1%)	Ointment	Topical ophthalmic	1 to 3 times daily; during the initial 24 to 48 hours, the frequency may be increased to every 4 hours	Care should be taken not to discontinue therapy prematurely.  If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.
FML Forte (fluoromethalone, 0.25%)	Suspension	Topical ophthalmic	2 to 4 times daily; during the initial 24 to 48 hours, the frequency may be increased to every 4 hours	Care should be taken not to discontinue therapy prematurely.  If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Flarex (fluoromethalone acetate, 0.1%)	Suspension	Topical ophthalmic	4 times daily; during the initial 24 to 48 hours, the frequency may be increased every 2 hours	Care should be taken not to discontinue therapy prematurely.  If there is no improvement after 2 weeks, the physician should be consulted.
Alrex (loteprednol etabonate, 0.2%)	Suspension	Topical ophthalmic	4 times daily	
Lotemax (loteprednol etabonate, 0.5%)	Suspension	Topical ophthalmic	<u>Postoperative inflammation:</u> 4 times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the post-operative period  <u>Steroid responsive disease:</u> 4 times daily; during the first week, the frequency may be increased up to every hour if needed	<u>Steroid responsive disease:</u> Care should be taken not to discontinue therapy prematurely.  If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.
Lotemax (loteprednol etabonate, 0.5%)	Gel	Topical ophthalmic	4 times daily beginning the day after surgery and continuing throughout the first 2 weeks of the post-operative period	
Lotemax (loteprednol etabonate, 0.5%)	Ointment	Topical ophthalmic	4 times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the post-operative period	
Pred Mild (prednisolone acetate, 0.12%)	Suspension	Topical ophthalmic	2 to 4 times daily; during the initial 24 to 48 hours, the frequency may be increased if necessary	Care should be taken not to discontinue therapy prematurely.  If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.
Omnipred (prednisolone acetate, 1%)	Suspension	Topical ophthalmic	4 times daily	Care should be taken not to discontinue therapy prematurely.  If signs and symptoms fail to improve after 2



Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				days, the patient should be re-evaluated.  In cases of bacterial infections, concomitant use of anti-infective agents is mandatory.
Pred Forte (prednisolone acetate, 1%)	Suspension	Topical ophthalmic	2 to 4 times daily; during the initial 24 to 48 hours, the frequency may be increased if necessary	Care should be taken not to discontinue therapy prematurely.  If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.
prednisolone sodium phosphate, 1%	Solution	Topical ophthalmic	Every hour during the day and every 2 hours during the night as necessary as initial therapy; reduce to every 4 hours when a favorable response is observed; later, further reduction to 3 to 4 times daily may suffice to control symptoms	The duration of treatment will vary with the type of lesion and may extend from a few days to several weeks.

See the current prescribing information for full details

## CONCLUSION

- Ophthalmic corticosteroids are used to treat a wide variety of ocular conditions of the conjunctiva, cornea, and anterior segment. These products exert anti-inflammatory activity against inciting agents of mechanical, chemical, or immunological nature.
- The anti-inflammatory potencies of the ophthalmic corticosteroid products depend on the pharmacokinetic and pharmacodynamic properties of both the drug and its formulation.
- Comparative data among the various ophthalmic corticosteroids are limited by the small numbers of trials, small sample sizes, and flaws in study design.
- Based on limited data, “soft” ophthalmic corticosteroids appear to be associated with less IOP-elevating potential compared with “strong” steroids, which are indicated for severe inflammation.
- Clinical guidelines address the use of ophthalmic corticosteroids post-operatively and for various conditions including anterior uveitis, bacterial keratitis, conjunctivitis, blepharitis, and dry-eye syndrome (AAO 2013a, AAO 2013b, AAO 2013c, AAO 2013d, Alexander et al 2004, Chuck et al 2018, Murrill et al 2004, Olson et al 2017, Quinn et al 2007).

## REFERENCES

- Alexander KL, Dul MW, Lalle PA, Magnus DE, Onofrey B. American Optometric Association: Optometric Clinical Practice Guideline – Care of the patient with anterior uveitis. <https://www.aao.org/documents/optometrists/CPG-7.pdf>. Reviewed 2004. Accessed April 9, 2018.
- Alrex [package insert], Bridgewater, NJ: Bausch + Lomb; May 2016.
- American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern Guidelines. Bacterial keratitis. <https://www.aao.org/preferred-practice-pattern/bacterial-keratitis-ppp--2013>. Updated 2013b. Accessed April 9, 2018.
- American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern Guidelines. Blepharitis. <https://www.aao.org/preferred-practice-pattern/blepharitis-ppp--2013>. Updated 2013c. Accessed April 9, 2018.
- American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern Guidelines. Dry eye syndrome. <https://www.aao.org/preferred-practice-pattern/dry-eye-syndrome-ppp--2013>. Updated 2013d. Accessed April 9, 2018.
- American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern Guidelines. Conjunctivitis. <https://www.aao.org/preferred-practice-pattern/conjunctivitis-ppp--2013>. Updated 2013a. Accessed April 9, 2018.
- Bielory BP, Perez VL, Bielory L. Treatment of seasonal allergic conjunctivitis with ophthalmic corticosteroids: in search of the perfect ocular corticosteroids in the treatment of allergic conjunctivitis. *Curr Opin Allergy Clin Immunol*. 2010;10(5):469-477.

- Chuck RS, Jacobs DS, Lee JK, et al; American Academy of Ophthalmology Preferred Practice Pattern Refractive Management/Intervention Panel. Refractive errors & refractive surgery preferred practice pattern. *Ophthalmology*. 2018;125(1):P1-P104.
- Chuck RS, Jacobs DS, Lee JK, et al; American Academy of Ophthalmology Preferred Practice Pattern Refractive Management/Intervention Panel. Refractive errors & refractive surgery preferred practice pattern. *Ophthalmology*. 2018;125(1):P1-P104.
- Comstock TL, Paterno MR, Singh A, Erb T, Davis E. Safety and efficacy of loteprednol etabonate ophthalmic ointment 0.5% for the treatment of inflammation and pain following cataract surgery. *Clin Ophthalmol*. 2011;5:177-186.
- Controlled evaluation of loteprednol etabonate and prednisolone acetate in the treatment of acute anterior uveitis. Loteprednol Etabonate US Uveitis Study Group. *Am J Ophthalmol*. 1999;127(5):537-544.
- Dexamethasone sodium phosphate ophthalmic solution, 0.1% [package insert], Bridgewater, NJ: Bausch + Lomb; June 2016.
- Donnenfeld ED, Holland EJ, Solomon KD, et al. A multicenter randomized controlled fellow eye trial of pulse-dosed difluprednate 0.05% versus prednisolone acetate 1% in cataract surgery. *Am J Ophthalmol*. 2011;152(4):609-617.
- Drugs@FDA: FDA approved drug products. Food and Drug Administration Web site. <https://www.accessdata.fda.gov/scripts/cder/daf/>. Accessed April 9, 2018.
- Durezol [package insert], Fort Worth, TX: Alcon Laboratories, Inc.; April 2017.
- Facts & Comparisons. Facts & Comparisons Web site. Facts & Comparisons. Facts & Comparisons Web site. <https://fco.factsandcomparisons.com/>. Accessed April 9, 2018.
- Flarex [package insert], Fort Worth, TX: Alcon Laboratories, Inc.; March 2017.
- FML ointment [package insert], Irvine, CA: Allergan Inc.; February 2013.
- FML suspension [package insert, Irvine, CA: Allergan Inc.; February 2013.
- FML Forte [package insert], Irvine, CA: Allergan Inc.; February 2013.
- Foster CS, Davanzo R, Flynn TE, McLeod K, Vogel R, Crockett RS. Durezol (Difluprednate Ophthalmic Emulsion 0.05%) compared with Pred Forte 1% ophthalmic suspension in the treatment of endogenous anterior uveitis. *J Ocul Pharmacol Ther*. 2010;26(5):475-483.
- Hamrah P, Dana R. Allergic conjunctivitis: Management. UpToDate Web site. 2018. <https://www.uptodate.com>. Updated December 1, 2017. Accessed April 9, 2018.
- Lane SS, Holland EJ. Loteprednol etabonate 0.5% versus prednisolone acetate 1.0% for the treatment of inflammation after cataract surgery. *J Cataract Refract Surg*. 2013 ;39(2):168-173.
- Lotemax ointment [package insert], Bridgewater, NJ: Bausch + Lomb; August 2016.
- Lotemax ointment [package insert], Bridgewater, NJ: Bausch + Lomb; April 2011.
- Lotemax suspension [package insert], Bridgewater, NJ: Bausch + Lomb; September 2016.
- Maxidex [package insert], Fort Worth, TX: Alcon Laboratories, Inc.; November 2017.
- McGhee CN, Dean S, Danesh-Meyer H. Locally administered ocular corticosteroids: benefits and risks. *Drug Saf*. 2002;25(1):33-55.
- Murrill CA, Stanfield DL, VanBrocklin MD, et al. American Optometric Association: Optometric Clinical Practice Guideline – Care of the adult patient with cataract. <https://www.aoa.org/documents/optometrists/CPG-8.pdf>. Reviewed 2004. Accessed April 9, 2018.
- Olson RJ, Braga-Mele R, Chen SH, et al. Cataract in the adult eye preferred practice pattern. *Ophthalmology*. 2017;124(2):P1-P119.
- Omnipred [package insert], Fort Worth, TX: Alcon Laboratories, Inc.; October 2007.
- Oner V, Türkcü FM, Taş M, Alakuş MF, Işcan Y. Topical loteprednol etabonate 0.5% for treatment of vernal keratoconjunctivitis: efficacy and safety. *Jpn J Ophthalmol*. 2012;56(4):312-318.
- Orange Book: Approved drug products with therapeutic equivalence evaluations. Food and Drug Administration Web site. <https://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>. Accessed April 9, 2018.
- Pleyer U, Sherif Z. Corticosteroids in ophthalmology. *Ernst Schering Res Found Workshop*. 2002;(40):65-81.
- Pred Forte [package insert], Irvine, CA: Allergan Inc.; May 2017.
- Pred Mild [package insert], Irvine, CA: Allergan Inc.; May 2017.
- Prednisolone sodium phosphate ophthalmic solution, 1% [package insert], Tampa, FL: Bausch & Lomb Incorporated; January 2013.
- Quinn CJ, Mathews DE, Noyes RF, Oliver GE, Thimons Jr. JJ, Thomas RK. Care of the patient with conjunctivitis. <https://www.aoa.org/documents/optometrists/CPG-11.pdf>. Accessed April 9, 2018.
- Raizman MB, Donnenfeld ED, Weinstein AJ. Clinical comparison of two topical prednisolone acetate 1% formulations in reducing inflammation after cataract surgery. *Curr Med Res Opin*. 2007;23(10):2325-2331.
- Sheppard JD, Toyos MM, Kempen JH, Kaur P, Foster CS. Difluprednate 0.05% versus prednisolone acetate 1% for endogenous anterior uveitis: a phase III, multicenter, randomized study. *Invest Ophthalmol Vis Sci*. 2014;55(5):2993-3002.
- Stewart RS. Controlled evaluation of fluorometholone acetate and loteprednol etabonate in the treatment of postoperative inflammation following cataract surgery. *Invest Ophthalmol Vis Sci* 2004;45: E-Abstract 292.